AMENDMENT TO THE CLAIMS

Please amend claims 146, 153, 184, 187, 191, 197 and 200; withdraw claims 168-176, (claims 1, 110-167, 177-183, 186, 188-190, 192-199 having previously been withdrawn); cancel claims 201-203 (claims 2-109 having previously been canceled), and add claims 204 and 205 as follows:

1. (Withdrawn) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising:

administering to a mammalian subject having an abnormal brain region an agonist of a calcium-activated potassium channel, the agonist being other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to selectively increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and

administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claims 2-109 (Canceled).

110. (Withdrawn) The method of claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke, or ischemia.

111. (Withdrawn) The method of claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by stroke.

112. (Withdrawn) The method of claim 1, wherein the abnormal brain region is region of tumor tissue.

113. (Withdrawn) The method of claim 1, wherein the abnormal brain region is a region of benign tumor tissue.

114. (Withdrawn) The method of claim 1, wherein the abnormal brain region is a region of malignant tumor tissue.

115. (Withdrawn) The method of claim 1, wherein the abnormal brain region includes a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

116. (Withdrawn) The method of claim 1, wherein the agonist is NS1619.

117. (Withdrawn) The method of claim 1, wherein the agonist is 1-EBIO.

118. (Withdrawn) The method of claim 1, wherein the agonist is a guanylyl cyclase activator.

119. (Withdrawn) The method of claim 118, wherein the guanylyl cyclase activator is a metalloporphyrin.

120. (Withdrawn) The method of claim 119., wherein the metalloporphyrin is a zinc protoporphyrin or a tin protoporphyrin IX.

121. (Withdrawn) The method of claim 118, wherein the agonist is a guanylyl cyclase activating protein.

122. (Withdrawn) The method of claim 1, wherein the mammal is a human.

123. (Withdrawn) The method of claim 1, wherein the medicant is a therapeutic cytotoxic agent.

124. (Withdrawn) The method of claim 1, wherein the medicant is cisplatin.

125. (Withdrawn) The method of claim 1, wherein the medicant is carboplatin.

126. (Withdrawn) The method of claim 1, wherein the medicant is methotrexate.

127. (Withdrawn) The method of claim 1, wherein the medicant is 5-fluorouracil.

128. (Withdrawn) The method of claim 1, wherein the medicant is amphotericin.

129. (Withdrawn) The method of claim 1, wherein the medicant is daunorubicin.

130. (Withdrawn) The method of claim 1, wherein the medicant is doxorubicin.

131. (Withdrawn) The method of claim 1, wherein the medicant is vincristine.

132. (Withdrawn) The method of claim 1, wherein the medicant is vinblastine.

133. (Withdrawn) The method of claim 1, wherein the medicant is busulfan.

134. (Withdrawn) The method of claim 1, wherein the medicant is chlorambucil.

135. (Withdrawn) The method of claim 1, wherein the medicant is cyclophosphamide.

136. (Withdrawn) The method of claim 1, wherein the medicant is melphalan.

137. (Withdrawn) The method of claim 1, wherein the medicant is ethyl ethanesulfonic acid.

138. (Withdrawn) The method of claim 1, wherein the medicant is a protein.

139. (Withdrawn) The method of claim 1, wherein the medicant is an antimicrobial agent or antibiotic.

140. (Withdrawn) The method of claim 1, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

141. (Withdrawn) The method of claim 1, wherein the medicant is a cytokine, cytokine agonist or cytokine antagonist.

142. (Withdrawn) The method of claim 141, wherein the cytokine is an interferon.

143. (Withdrawn) The method of claim 141, wherein the cytokine is a transforming growth factor.

144. (Withdrawn) The method of claim 143, wherein the transforming growth factor is transforming growth factor-β.

145. (Withdrawn) The method of claim 141, wherein the cytokine is tumor necrosis factor-α.

146. (Withdrawn-Currently Amended) The method of claim 141, wherein the cytokine is a an interleukin.

147. (Withdrawn) The method of claim 1, wherein the cytokine is interleukin-2.

148. (Withdrawn) The method of claim 1, wherein the medicant is an immunotoxin and immunosuppressive.

149. (Withdrawn) The method of claim 1, wherein the medicant is a boron compound.

150. (Withdrawn) The method of claim 1, wherein the medicant is an adrenergic agent.

151. (Withdrawn) The method of claim 1, wherein the medicant is an anticonvulsant.

152. (Withdrawn) The method of claim 1, wherein the medicant is an ischemia-protective agent.

153. (Withdrawn - Currently Amended) The method of claim 152, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist.

154. (Withdrawn) The method of claim 1, wherein the medicant is an antitrauma agent.

155. (Withdrawn) The method of claim 1, wherein the medicant is a diagnostic agent.

156. (Withdrawn) The method of claim 1, wherein administering the agonist is by intravenous or intra-arterial infusion or injection.

157. (Withdrawn) The method of claim 1, wherein administering the agonist is by intracarotid infusion or injection.

158. (Withdrawn) The method of claim 1, wherein the agonist is administered to the mammalian subject by a bolus injection.

159. (Withdrawn) The method of claim 1, wherein the agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

160. (Withdrawn) The method of claim 159, wherein the agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

161. (Withdrawn) The method of claim 159, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

162. (Withdrawn) The method of claim 159, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu g\ kg^{-1}\ min^{-1}$.

163. (Withdrawn) The method of claim 1, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

164. (Withdrawn) The method of claim 1, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

165. (Withdrawn) A method of selectively delivering a medicant to an abnormal brain region in a mammalian subject, comprising:

administering to a mammalian subject having an abnormal brain region an agonist of a calcium-activated potassium channel, the agonist being other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase potassium flux through a calcium-activated potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to cells of the abnormal brain region, whereby the capillary or arteriole is made more permeable to the medicant; and

administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

166. (Withdrawn) The method of claim 165, wherein the medicant is a cytokine, cytokine agonist or cytokine antagonist.

167. (Withdrawn) The method of claim 165, wherein the cytokine is interleukin-2,

168. (Withdrawn) A pharmaceutical composition comprising a combination of an agonist of a calcium-activated potassium channel, the agonist being other than bradykinin or a bradykinin analog, formulated in a pharmaceutically acceptable solution together with a therapeutic cytotoxic agent for delivery by intravascular infusion or injection into a mammal.

169. (Withdrawn) The pharmaceutical composition of claim 168, wherein the agonist is present in an amount of about 0.075 to 1500 micrograms per kilogram body mass.

170. (Withdrawn) The pharmaceutical composition of claim 168 wherein the agonist is present in an amount of about 0.075 to 150 micrograms per kilogram body mass.

171. (Withdrawn) The pharmaceutical composition of claim 168, wherein the agonist is NS1619.

172. (Withdrawn) The pharmaceutical composition of claim 168, wherein the agonist is 1-EBIO.

173. (Withdrawn) The pharmaceutical composition of claim 168, wherein the agonist is a guanylyl cyclase activator.

174. (Withdrawn) The pharmaceutical composition of claim 173, wherein the guanylyl cyclase activator is a metalloporphyrin.

175. Withdrawn) The pharmaceutical composition of claim 174, wherein the metalloporphyrin is a zinc protoporphyrin or a tin protoporphyrin IX.

176. (Withdrawn) The pharmaceutical composition of claim 168, wherein the agonist is a guanylyl cyclase activating protein.

177. (Withdrawn) The pharmaceutical composition of claim 168, wherein the therapeutic cytotoxic agent is cisplatin.

178. (Withdrawn) The pharmaceutical composition of claim 168, wherein the therapeutic cytotoxic agent is carboplatin.

179. (Withdrawn) The pharmaceutical composition of claim 168, wherein the therapeutic cytotoxic agent is methotrexate.

180. (Withdrawn) The pharmaceutical composition of claim 168, wherein the therapeutic cytotoxic agent is 5-fluorouracil.

181. (Withdrawn) The pharmaceutical composition of claim 168, wherein the therapeutic cytotoxic agent is amphotericin.

182. (Withdrawn) The method of claim 168, wherein the therapeutic cytotoxic agent is daunorubicin, doxorubicin, vincristine, or vinblastine.

183. (Withdrawn) The pharmaceutical composition, of claim 168, wherein the therapeutic cytotoxic agent is busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

184. (Currently Amended) A pharmaceutical composition comprising a combination of an agonist of a calcium-activated potassium channel formulated

together in a pharmaceutically acceptable solution with a drug for delivery by intravascular infusion or injection,

wherein the drug is a protein, antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anti-convulsant, anti-trauma agent or diagnostic agent, and

wherein the agonist is selected from the group consisting of NS-1619, 1-EBIO, guanylyl cyclase activating protein and combinations thereof.

185. (Previously Presented) The pharmaceutical composition of claim 184, wherein the drug is a protein.

186. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an antimicrobial agent or antibiotic.

187. (Currently amended) The pharmaceutical composition of claim 184, wherein the drug is~~,~~ a cytokine, a cytokine agonist or a cytokine antagonist.

188. (Withdrawn) The pharmaceutical composition claim 184, wherein the cytokine is an interferon.

189. (Withdrawn) The pharmaceutical composition of claim 187, wherein the cytokine is a transforming growth factor.

190. (Withdrawn) The pharmaceutical composition of claim 187, wherein the cytokine is tumor necrosis factor-α.

191. (Currently Amended) The pharmaceutical composition of claim 187, wherein the cytokine is ~~a~~ an interleukin.

192. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an immunotoxin or immunosuppressant.

193. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is a boron compound.

194. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an adrenergic agent.

195. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an anticonvulsant.

196. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an ischemia-protective agent.

197. (Withdrawn-Currently Amended) The pharmaceutical composition of claim 196, wherein the drug is a N-methyl-D-aspartate (NMDA) receptor antagonist.

198. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is an antitrauma agent.

199. (Withdrawn) The pharmaceutical composition of claim 184, wherein the drug is a diagnostic agent.

200. (Currently Amended) A kit for enhancing the delivery of a medicant to an abnormal brain region, comprising:

an agonist of a calcium-activated potassium channel, said agonist being other than bradykinin or a bradykinin analog and is selected from the group consisting of NS-1619, 1-EBIO, guanylyl cyclase activating protein and combinations thereof;

a medicant; and

instructions for using the agonist for enhancing the delivery of a the medicant to an abnormal brain region by increasing the permeability of a capillary or arteriole delivering blood to cells of the abnormal brain region.

Claims 201-203 (Canceled).

204. (New) A pharmaceutical composition comprising a combination of an agonist of a calcium-activated potassium channel, other than a metalloporphyrin, formulated together in a pharmaceutically acceptable solution with a drug for delivery by intravascular infusion or injection,

wherein the drug is a protein, antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anti-convulsant, anti-trauma agent or diagnostic agent.

205. (New) A kit for enhancing the delivery of a medicant to an abnormal brain region, comprising:

an agonist of a calcium-activated potassium channel, said agonist being other than bradykinin, a bradykinin analog, or a metalloporphyrin;

a medicant; and

instructions for using the agonist for enhancing the delivery of the medicant to an abnormal brain region by increasing the permeability of a capillary or arteriole delivering blood to cells of the abnormal brain region.